

We claim:

1. A method of identifying an effective agent that dissociates nuclear hormone receptor activities, comprising the steps of:

5 (a) contacting a nuclear hormone receptor with one or more agents under conditions suitable for forming a test complex comprising nuclear hormone receptor dimer, coactivator and corepressor;

10 (b) assaying for coactivator association with said test complex; and

(c) assaying for corepressor association with said test complex,

15 wherein coactivator association combined with corepressor association indicates that at least one of said agents is an effective agent that dissociates nuclear hormone receptor activities.

2. A method of identifying an effective agent that dissociates nuclear hormone receptor activities, comprising the steps of:

5 (a) contacting a nuclear hormone receptor with one or more agents under conditions suitable for forming a ternary complex comprising nuclear hormone receptor dimer, bound cognate response element, coactivator and corepressor;

10 (b) assaying for coactivator association with said ternary complex; and

(c) assaying for corepressor association with said ternary complex,

15 wherein coactivator association combined with corepressor association indicates that at least one of said agents is an effective agent that dissociates nuclear hormone receptor activities.

3. The method of claim 1, wherein said contacting is performed *in vitro*.

20 4. The method of claim 1, wherein said nuclear hormone receptor is contacted with said one or more agents in the presence of a eukaryotic cell sample.

5. The method of claim 4, wherein said eukaryotic cell sample comprises viable cells.

25 6. The method of claim 4, wherein said eukaryotic cell sample comprises a whole cell lysate.

7. The method of claim 4, wherein said eukaryotic cell sample comprises a fractionated cell lysate.

8. The method of claim 4, wherein said eukaryotic cell sample comprises an exogenous nucleic acid molecule encoding said nuclear hormone receptor.

9. The method of claim 4, wherein said coactivator is endogenous to said cell.

10. The method of claim 4, wherein said corepressor is endogenous to said cell.

11. A method of identifying an effective agent that dissociates nuclear hormone receptor activities, comprising the steps of:

(a) contacting a nuclear hormone receptor with one or more agents under conditions suitable for forming a test complex comprising nuclear hormone receptor dimer, coactivator and corepressor,

wherein said nuclear hormone receptor is selected from the group consisting of a retinoic acid receptor, retinoid X receptor, thyroid receptor, estrogen receptor and peroxisome proliferator activated receptor;

(b) assaying for coactivator association with said test complex; and

(c) assaying for corepressor association with said test complex,

wherein coactivator association combined with corepressor association indicates that at least one of said agents is an effective agent that dissociates nuclear hormone receptor activities.

5 12. The method of claim 11, wherein said nuclear hormone receptor is selected from the group consisting of RAR α , RAR β , RAR γ , RXR α , RXR β and RXR γ .

10 13. The method of claim 12, wherein said nuclear hormone receptor is a retinoic acid receptor selected from the group consisting of RAR α , RAR β and RAR γ .

 14. The method of claim 1, wherein said coactivator is selected from the group consisting of

15 SRC-1/NCoA-1;
 TIF-2/GRIP-1/NCoA-2;
 ACTR/p/CIP/AIB1/NCoA-3;
 p300/CBP;
 p/CAF; and
 TATA box binding protein.

20 15. The method of claim 14, wherein said coactivator is SRC-1/NCoA-1.

 16. The method of claim 1, wherein said corepressor is selected from the group consisting of N-CoR and SMRT.

25 17. The method of claim 16, wherein said corepressor is N-CoR.

18. A method of identifying an effective agent that dissociates nuclear hormone receptor activities, comprising the steps of:

5 (a) contacting a nuclear hormone receptor with one or more agents under conditions suitable for forming a test complex comprising nuclear hormone receptor dimer, coactivator and corepressor;

10 (b) assaying for coactivator association with said test complex, wherein said coactivator is selected from the group consisting of SRC-1/NCoA-1, TIF-2/GRIP-1/NCoA-2, ACTR/p/CIP/AIB1/NCoA-3, p300/CBP, p/CAF, and TATA box binding protein (TBP); and

15 (c) assaying for corepressor association with said test complex, wherein said corepressor is selected from the group consisting of N-CoR and SMRT,

wherein coactivator association combined with corepressor association indicates that at least one of said agents is an effective agent that dissociates nuclear hormone receptor activities.

20 19. The method of claim 1, wherein step (b) comprises specific binding to said test complex.

20. The method of claim 19, wherein step (b) comprises immunoprecipitation of said test complex.

25 21. The method of claim 20, wherein said immunoprecipitation is performed using antibody immunoreactive with said nuclear hormone receptor dimer.

22. The method of claim 19, wherein step (b) comprises immunodetection of said coactivator.

23. The method of claim 1, wherein step (c) comprises specific binding to said test complex.

5 24. The method of claim 23, wherein step (c) comprises immunoprecipitation of said test complex.

25. The method of claim 24, wherein said immunoprecipitation is performed using antibody immunoreactive with said nuclear hormone receptor dimer.

10 26. The method of claim 23, wherein step (c) comprises immunodetection of said corepressor.